REMARKS

Claims 54, 56, 60-64, 66, 67, 69, 72, 73 and 76-86 are pending. Independent claims 54 and 82 have been amended to recite that the polynucleotide transiently replicates in the cytoplasm of the plant cell.

The main thrust of the present invention is to provide a cancer patient with a tumor-specific vaccine before the patient dies. The present invention directly infects many plants with the claimed polynucleotide vector and is ready for harvesting all of the plants, with essentially complete infection, in a week. Viral infection in a whole plant (or acres of plants) is very quick. By contrast, producing a similar mass of cells by cell mammalian or insect cell culture requires a long period of time for many generations of replication after a different vector integrates into the genome and the appropriate cell is selected. Producing a comparable number of transgenic plants requires using a different vector to integrates into a plant cell genome followed by selecting transgenic cells, followed by regenerating an entire plant from a single cell, followed by harvesting and planting the seeds to make a large number of plants which are ready for harvesting. This time is measured from months to crop seasons. Timeliness is critical to the patient with cancer.

The presently claimed invention recites a polynucleotide that has the properties of the plant infecting viral vector, not a vector for integrating to produce a transgenic plant or animal cell.

Claims 54, 56, 60-64, 66, 67, 69, 72, 73 and 77-80 were rejected under 35 USC 103(a) as being unpatentable over Casper et al in view of Fiedler et al and Ladner. Casper et al produce their idiotype scFV in mammalian or insect cells and offer no suggestion that it is even possible to produce a suitable vaccine in plant cells, much less providing any suggestion of how. Additionally, their product required an adjuvant to induce any immunity. Furthermore, Casper et al uses only one linker, $(Gly_3Ser_1)_4$, which is outside the scope of the present claims. Fiedler et al produce a single chain antibody in transgenic plants. The single chain antibody is not taught to be capable of inducing an immune response. As with Casper et al, Fiedler et al uses a different linker from that claimed. Ladner teaches using a computer method to determine an acceptable linker for a single chain antibody and subsequently making such a single chain antibody. This rejection is respectfully traversed.

Even combined these references do not disclose certain claim recitations. No combination of these references suggests such claim recitations. Present claims 54 and 82 have been amended to recite a polynucleotide, which includes a sequence for allowing the polynucleotide to replicate transiently in the cytoplasm of the plant cell. None of the references discloses a polynucleotide replicating in the cytoplasm of the cell. All replication of the polynucleotide in question in the reference occurs in the cell nuclei. Also, expression of the single chain antibodies in the references is essentially constitutive. This is quite different from the present invention where normal plants are grown and then one infects the plant with a virus carrying the claimed polynucleotide, which infects many cells in the plant.

The only reference suggesting any polynucleotide in any plant cell is Fiedler et al who prepare a transgenic plant where their polynucleotide is first integrated into the plant genome of a cell followed by regenerating an entire plant from that cell. The Fiedler et al polynucleotide is neither replicating in the plant cell cytoplasm, nor is it transient. The taught integrating vector is a different type of construct and expresses in a different manner from the infecting virus of the present invention. These features are presently claimed. Accordingly, there is no suggestion that the B-cell lymphoma surface immunoglobulin antigen of the present invention would be expressible at all or in the same fashion, thereby rendering the claimed polynucleotide unobvious.

No combination of these references suggests that one could make an immunogenic B-cell lymphoma surface immunoglobulin antigen in plant cells which would induce immunity, particularly without an adjuvant. Note the recent publications attached as exhibits in the previous response. The importance of this embodiment is apparently recognized by the examiner, as claims previously containing such language (81-86) were not rejected. Applicants wish to point out an apparent oversight because dependant claim 72 also has such language.

The antibody produced by Caspar et al is not produced in plant cells and requires an adjuvant to induce any type of immune response (whether protective or not). Fiedler et al and Ladner do not suggest and are completely unconcerned with whether their single chain antibodies are capable of inducing any immune response at all, since nothing similar is mentioned in them. The examiner's assertion that the Fiedler et al "scFV is functionally active" is completely misplaced because no immunogenic activity is ever detected. Even combined, the references do not provide any teaching of producing any immunogenic protein in plants, much less the claimed B-cell lymphoma surface immunoglobulin antigen that induces immunity without an adjuvant.

Still further, many claims (e.g. 67, 77) recite that the claimed polynucleotide contains a randomized linker between the domains. The randomized linker library contains structures different from those conventionally used, including those conventional linkers in the references. None of the references discloses a randomized linker. All of the references use a predetermined linker. All references disclose a single fixed linker which is either conventional or one determined by a computer method. The examiner's assertion that using "any linker" would be obvious cannot include a randomized library of linkers as this is contradicted by the references themselves which either use a conventional linker or one determined to be optimum by the Ladner method.

It should be noted that Ladner is optimizing his linker to produce a single chain antibody for binding to an antigen, a different function from the present invention. (See claim 77) Applicants assert that the field of making a vaccine is still unpredictable as demonstrated by the numerous unsuccessful attempts at making vaccines against a large number of diseases (such as HIV) in spite of considerable effort. Computer generated methods for producing a single chain antibody linker optimized to a different use is of little value in suggesting the present invention.

Accordingly, because the claimed polynucleotide is different in:

1) its claimed structures and abilities to replicate,

2) its claimed structure and abilities to induce an immune response and

3) its claimed structure and abilities regarding the linker,

the rejection should be withdrawn.

Applicants wish to thank the examiner for indicating that Claim 76 contains allowable subject matter if rewritten in independent form. Applicants also note that claims 81-86 were not rejected, apparently containing allowable subject matter. Claim 82 is in independent form and is thus now clearly in condition for allowance.

If there are any other remaining issues to be resolved, the examiner is encouraged to telephone the undersigned for prompt resolution.

CONCLUSIONS

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance of claims 54, 56, 60-64, 66, 67, 69, 72, 73 and 76-86 are respectfully requested.

The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No. 500933.

Respectfully submitted,

February 17, 2004

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